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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,006	03/28/2005	Shirou Sawa	2005_0232A	1756

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EXAMINER	
THOMAS, TIMOTHY P	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,006	SAWA ET AL.	
	Examiner	Art Unit	
	Timothy P. Thomas	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-40* is/are pending in the application.

4a) Of the above claim(s) *39 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :2/17/2005, 4/11/2005, 7/12/2007.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group I, claims 19-38 in the reply filed on 8/20/2007 is acknowledged.

2. Applicant's election without traverse of claim 20 as the alkyl aryl polyether alcohol type polymer or polyethylene glycol fatty acid ester species (interpreted as tyloxapol, contained in the claim) in the reply filed on 8/20/2007 is acknowledged.

3. Claims 39-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/20/2007.

Status of Claims

4. Claims 19-40 are pending. Claims 39-40 are withdrawn. Claims 19-38 are examined on the basis of the merits.

Priority

5. Applicant is advised of possible benefits Applicant is advised of possible benefits under 35 U.S.C. 119(a)-(d), wherein an application for patent filed in the United States may be entitled to the benefit of the filing date of a prior application filed in a foreign country.

6. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Acknowledgement is made of applicant's claim to foreign priority and the receipt of a copy of the application, JP2003-012427, filed 1/21/2003. However, since no

translation has been provided, prior art dates have been determined with reference to the priority date for the PCT application date, PCT/JP04/00350, filed 1/16/2004.

Oath/Declaration

7. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It was not executed in accordance with either 37 CFR 1.66 or 1.68.

The oath or declaration contains no signatures of the inventors with date signed

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 19-24 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Gamache, et al. (WO 01/15677 A2; 03/2001).

Gamache teaches all of the components of the claims: compositions for otic and intranasal use (p.6, lines 5-6) that contain a combination of a 5-HT agonist and an anti-

inflammatory agent (p. 6, lines 1-4; p. 12 lines 9-10) or alternatively sequential or concurrent dosing of separate compositions that contain the 5-HT antagonist in one composition and the anti-inflammatory agent in a second composition (p. 12, lines 9-11); specifically claimed is the anti-inflammatory specie bromfenac (the first compound of instant claim 19; claim 11;); typical concentrations of anti-inflammatory agents, such as bromfenac, are taught in the range 0.01-1.0 % (w/v) (overlapping with 0.01-0.5; p. 13, lines 6-8); aqueous formulations are preferred (p. 10, lines 11-14); tyloxapol is taught at the concentration of 0.05 % (w/v) (p. 16, line 30). It is noted that claim 21 and further dependent claims limit the options for the salt of bromfenac to the sodium salt, and that the specific concentrations recited in dependent claims apply to the sodium salt; the other options (bromfenac or a hydrate of bromfenac) are still viable choices that are part of the claims 21 and dependent claims (which depend on and include the options of claim 20). Gamache anticipates 1) the claim to bromfenac in the concentration range of claim 20 (which is also an option of claims 21-24 and 31). 2) The form of bromfenac in solution will be the same when the acid is dissolved in a solution followed by adjustment to the desired pH with NaOH/HCl (Gamache, p. 15, line 33) as when the sodium salt is dissolved in solution adjusted to the same pH; for this case Gamache also anticipates the sodium salt limitation of claim 21, albeit not the sodium salt concentration limitation of claim 22 and further dependent claims, since the claim is drawn to an aqueous liquid preparation, irrespective of how it is prepared.

10. Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Dobrozsi (US 6,319,513 B1; 11/2001).

Dobrozsi teaches aqueous liquid compositions comprising a pharmaceutically active agent selected from a group that includes analgesics (abstract); a specie taught is bromfenac (column 10, line 11); tyloxapol is taught at 0.15 and 0.035 % (Example 10).

11. Claims 19-38 are rejected under 35 U.S.C. 102(e) as being anticipated by Sawa (US 2007/0082857 A1; priority date 11/2003).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Sawa teaches the elements of the claims: aqueous solution preparations comprising an aminoglycoside antibiotic and bromfenac or a salt of bromfenac (abstract); bromfenac sodium and bromfenac sodium hydrate is taught at 0.1 and 0.2 % (Tables 1, 3, 6, 9-15); tyloxapol at 0.3 % resulted in solutions that were clear, when the control (no additive) was turbid (Table 5, 8), tyloxapol is also taught at 0.02 % (Table 15); additives taught include benzalkonium chloride (Table 8), boric acid (Tables 9, 12), sodium edentate (Table 15), and sodium hydroxide (Table 15); pH values include 7.5, 7.8 and 8.0 (Tables 9-15); eye drop formulations are also taught (Examples 1-7). It is noted that the aqueous preparations contain an active ingredient not in the instant

claims. However, Sawa still anticipates the instant claims, due to the open language construction of the claims (use of "comprising").

12. Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 19-29, 31-34, and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gamache, et al. (WO 01/15677 A2; 03/2001) and ISTA Pharmaceuticals ("New Drug Applications: Xibrom", http://www.drugs.com/nda/xibrom_040525.html, accessed online 9/19/2007) or Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenic in rodents:; Agents and Actions; 1988 Aug; 25(1-2):77-85, abstract).

Claims 19-24 and 31 are rejected as outlined above. With respect to claims 21-38 (claims 21-24 and 31, with respect to the sodium salt of bromfenic and associated concentrations), in addition to the points made above, Gamache also teaches the additives and pH of the instant claims, edetate disodium, benzylalkonium chloride, sodium hydroxide, and a pH of 7.3-7.4 (Example 2); polyvinyl pyrrolidone (p. 14, line 5); and sodium borate buffer (p. 13, line 11). Gamache does not specifically teach the sodium salt of bromfenic, nor a hydrate, nor the concentration range or specific bromfenic sodium concentrations of 0.05-0.2, or at 0.1 or 0.2 %, nor the tyloxapol concentrations of 0.02 or 0.3 %. The ISTA Pharmaceuticals news release demonstrates that products containing 0.1 % bromfenac sodium acquired US marketing rights for Xibrom in May 2002 (were known by others in this country before applicant's priority date, a 35 USC 102(a) date). Nolan teaches bromfenac (the sodium salt, sesquihydrate form) was effective as a topical analgesic at concentrations of 0.1-0.32 % in mice and more potent than the other drugs tested (abstract). It would have been

obvious for one of ordinary skill in the art at the time of the invention to select concentrations of bromfenac sodium, sesquihydrate of 0.1, about 0.2 and about 0.32 %, in the invention of Gamache, since these values have demonstrated efficacy for topical use. It would have been obvious to adjust the concentration of tyloxapol, to see what the effect would be on the solubility and stability of the aqueous preparations, which would have resulted in the effective concentrations of the instant claims. It would also have been obvious to adjust the pH to values in the 7.5 to 8.5 range, with the potential of dissolving and/or stabilizing more of the acidic drug, bromfenic, in a more aqueous soluble ionic form. The motivation would have been to prepare pharmaceutical products with optimal drug dosage and stability.

17. Claims 19-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yakuji Nippo Ltd. ("New Drugs in Japan"; 2001; English translation provided; IDS Reference AP) and Xia (US 6,369,112 B1).

Yakuji Nippo teaches a bromfenac sodium sesquihydrate ophthalmic formulation that contains: 0.1% (w/v) bromfenac (items 1-3); boric acid buffer, sodium sulfite, disodium eentate, polyvinylpyrrolidone, and benzalkonium chloride (item 2, additives); a pH of 8.0-8.6 (item 2, pH). Yakuji Nippo does not teach tyloxapol. Xia teaches a solution useful for contact lenses that provides enhanced cleaning and disinfecting efficacy of the contact lens (abstract), which contains tyloxapol as one of three ingredients (abstract; column 3, lines 7-21); tyloxapol is taught at concentrations of 0.25 and 0.025 (about 0.02 and 0.3; Table 1). Xia teaches the addition of tyloxapol to the solution improves the stability and therefore the disinfecting efficacy over time of the

active component (column 7, lines 8-18). It would have been obvious to one of ordinary skill in the art at the time of the invention to add tyloxapol to the ophthalmic formulation of Yakuji Nippo. The motivation to do so is that taught by Xia, the stability enhancing effect of this component on the active ingredient. There would have been an expectation of success, since tyloxapol has demonstrated efficacy with the contact lens cleaning solutions.

18. Claim19-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yakuji Nippo Ltd. ("New Drugs in Japan"; 2001; English translation provided; IDS Reference AP) and Xia (US 6,369,112 B1) as applied to claims 19-30 above, and further in view of Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenic in rodents:; Agents and Actions; 1988 Aug; 25(1-2):77-85, abstract).

Neither Yakuji Nippo or Xia teach the bromfenac sodium hydrate solutions at a bromfenac concentration of 0.2 %. Nolan teaches topical solutions are efficacious in the concentration range of 0.1-0.32 %. It would have been obvious to one of ordinary skill in the art at the time of the invention to use a concentration of about 0.2% bromfenic sodium hydrate (right in the middle of the range Nolan teaches is effective), in the modified Yakuji Nippo ophthalmic solution with tyloxapol added. The motivation to use a higher bromfenac concentration would be to provide an option of a more concentrated solution for patients in cases where a physician determines that higher anti-inflammatory concentration is desirable, such as when the lower dosage does not completely relieve the inflammation or pain.

Double Patenting

19. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. Claims 19-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending Application No. 11/755662. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application contains claims drawn to method of treating pain and/or inflammation associated with an ocular condition, by administering the aqueous solutions of the instant claims. It would have been obvious to one of ordinary skill in the art at the time of the invention to use the formulations of the instant claims in the methods of the copending application, since the claims recite that the formulations are eye drops, and the instant abstract also teaches some of the conditions treated of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

21. No claim is allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy P. Thomas whose telephone number is (571) 272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TPT/

Timothy P. Thomas
Patent Examiner

9/22/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER